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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,148	03/01/2004	Amedeo Leonardi	04266/100M619-US3	3142
7278	7590	07/29/2005	EXAMINER	
DARBY & DARBY P.C.			GEMBEH, SHIRLEY V	
P. O. BOX 5257			ART UNIT	PAPER NUMBER
NEW YORK, NY 10150-5257			1614	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/791,148

Applicant(s)

LEONARDI ET AL.

Examiner

Shirley V. Gembeh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-71 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>04/15/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The information disclosure statement (IDS) submitted on April 15, 2005, has been considered.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 and 67-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaviraghi et al., US 6,071,939, Sada et al., US 6,878,703 B2 in view of New drug evaluation, No. 20, April 1998, Gasser et al., 1999 J. Clinical and Basic Cardiology (2)

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169-174 and Norwood et al., Drug forecast, Olmesartan Medoxomil for hypertension: A clinical review.

Gaviraghi et al., teach a method of treating hypertension (claim 1) administering an angiotensin II receptor (claims 1, 8, 11 and 13)(column 1 line 19-20) antagonist (telmisartan column 1 line 19) and a calcium channel blocker (claim 1) lacidipine (column 1 line 14). The patent teaches combination of lacidipine and telmisartan provided an unexpectedly advantageous combination for the treatment of hypertension column 1 lines 30+. Gaviraghi et al., also teach of the dosage range of the angiotensin II receptor blocker (claims 4, 9, 14, 21, 29, 32, 40, 43, 50 and 56) to be 10mg- 100mg and the calcium channel blocker to be 1-6mg at column 3 lines 39+, see claim 9 (i) as disclosed by applicant, and is taught at column 3 lines 40+ of the patent.

However, Gaviraghi et al., did not teach the administering the drugs as disclosed by applicant in claims 3, 4, 9, 14, 21, 29, 32, 40, 43, 50 and 56 nor teach the diuretic of claims 2, 6-7, 67-71.

Sada et al., teach administering an angiotensin II receptor antagonist (claim 1) and a diuretic (claims 2, 6-7, 67-71) for the treatment of hypertension column 1 lines 13+, where the diuretic is a chlorthalidone (claims 6, 7, 18, 36, 37, 70-71) (column 4 line 54) or a hydrochlorothiazide (column 4 line 58)(claims 6, 7, 36, 37, 68-69).

New Drug evaluation teaches lercanidipine administered to mild –moderate hypertension patients at 10mg or 20 mg daily (see page 1 of reference).

Gasser et al., teach administering lercanidipine as low as 5 mg/day (page 171 therapeutic use) to 40mg/day.

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Drug forecast teach administering olmesartan medoxomil as in claim 3, for treatment of hypertension at dosages ranging from 2.5-80 mg as shown on page 614 (clinical efficacy) and table 2 of the same page. Drug forecast also teach irbesartan, telmisartan (same drug taught by Gaviraghi) are also angiotensin II receptor blockers and the dosage on page 614 table 2 and also of irbesartan (claim 8) on the same page. The reference also teach hydrochlorothizide administered from 25-50mg/day page 614 second column-Puchler study lines 4+.

The claims differ where Gaviraghi uses telmisartan and lacidipine to treat hypertension instead of olmesartan and lercanidipine combination.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace the drug telmisartan and lacidipine as taught by Gaviraghi with that of olmesartan and lercanidipine as disclosed by Gasser and New Drug to provide for the treatment of hypertension. One of skill in the art would have known that using olmesartan and lercanidipine combination in place of lacidipine and telmisartan would work because each are well known drugs used for the treatment of hypertension. Telmisartan and olmesartan medoxomil are well known angiotensin II receptor drug that have the same function in the treatment of hypertension. Lacidipine and lercanidipine are functionally equivalent and are both calcium channel blockers in the treatment of hypertension. Gaviraghi also teaches that combining or co administration of telmisartan and lacidipine, gave a synergistic, antihypertensive effect, improvement of blood pressure control was achieved (see column 1 lines 35+).

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Gaviraghi et al., teach that telmisartan and lacidipine was used in treating hypertension, in patients to show the combinatory effect of the drug administered. The result showed significant reduction effect in the mean blood pressure and the heart rate (column 5 line 45-67) as obvious to the teachings to be responders. Although, this study did not per se teach the combination as disclosed by applicant, it teaches the use of an angiotensin II receptor blocker combine with a calcium channel blocker and how it affects hypertension.

Sada et el teach in addition to the angiotensin II receptor blocker a diuretic (as in claim 2) to be hydrochlorothiazide as in claim 6. It is known that co-administration of an angiotensin and a diuretic is an effective therapy for treatment of hypertension (column 1 lines 28+). Sada also teaches the effect of co-administration of the drug, in that the drugs switch on signals at their respective receptors to cause pharmacological actions (column 11 lines 47+), and cause the plasma concentration to decrease.

One of ordinary skill in the art would have expected successful results in administering an angiotensin II receptor blocker together with a calcium channel blocker and a diuretic to treat hypertensive patients since both are successful separately. Therefore, one of ordinary skill would have been successful combining the teaching of the selection of olmesartan medoxomil and lercanidipine for the treatment of hypertension and using a diuretic. Diurectics have been used to treat hypertension patients. One of ordinary skill in the art would have combined the teaching of Gaviraghi with that of Sada, to lower the heart rate of the hypertensive individual or patient and thereby ameliorate hypertension. Both references teaches that combination of an

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angiotensin II receptor with a calcium channel blocker or using an angiotensin II receptor with a diuretic gave better result in lowering the blood pressure.

Further, one of skill would have been motivated to combine the teachings of Gaviraghi with that of Sada, New Drug, Gasser and Norwood as disclosed by administering the doses (in claims 4 etc) and expect a successful result in the treatment of hypertension. Using drug doses taught by Drug forecast (administering olmesartan medoxomil for hypertension at dosages ranging from 2.5-80 mg as shown on page 614) together with 25-50mg/day of the diuretic and lercanidipine from 5mg —40 mg as taught by Gasser, one skilled in the art would expect to treat various population of hypertensive patients with different combinations of olmesartan medoxomil/ lercanidipine and hydrochlorothiazide.

Claims 4, 9, 14, 21, 29, 32, 40, 43, 50 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaviraghi et al., US 6,071,939, Sada et al., US 6,878,703 B2 in view of New drug evaluation, No. 20, April 1998, Gasser et al., 1999 J. Clinical and Basic Cardiology (2) 169-174 and Norwood et al., Drug forecast, Olmesartan Medoxomil for hypertension: A clinical review as applied to claims 1-7 and 67-71 above, and further in view of Physicians Desk Reference (PDR) (C) Sanko Pharm Inc 2002.

While the combined references of Gaviraghi et al., Sada et al., New drug evaluation, No. 20, Gasser et al., Norwood et al., do not teach claims 4, 9, 14, 21, 29, 32, 40, 43, 50 and 56 wherein there are variation of administration of the first amount

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(an angiotensin II receptor blocker) and the second amount (calcium channel blocker), as olmesartan and lercanidipine.

The PDR teaches (see highlighted section) olmesartan medoximil on page 3 of reference (general) is administered up to 320 mg or given in multiple doses of up to 80 mg, (Claims 5) the reference also teach on page 5 angiotensin receptor blockers and hydrochlorthiazide had lowering effect of blood pressure.

Gaviraghi et al., also teach of the dosage range of the angiotensin II receptor blocker (claims 4, 9, 14, 21, 29, 32, 40, 43, 50 and 56) to be 10mg- 100mg and the calcium channel blocker to be 1-6mg at column 3 lines 39+, see claim 9 (i) as disclosed by applicant, and is taught at column 3 lines 40+ of the patent.

Since the PDR teaches the dosage range of olmesartan medoximil, one of ordinary skill in the art would combine the teachings of Gaviraghi with that of Sada, New Drug, Gasser and Norwood with that of PDR, and expect a successful result in varying or optimizing the doses, from mild to high hypertensive patients. Gaviraghi already teaches of the combinatory effect of telmisartan and lacidipine (see column 3 lines 39+) and column 2 lines 59 + where the patent teaches that the combination amount will vary according to the body weight, age, general condition and severity of the disease. One skill in the art would know that any combination of an angiotensin II receptor with a calcium channel blocker would be successful, as several variation of the combination already exist (see above discussion). With regards to the different population treated, as taught by Gaviraghi, column 2 line 59+ depending on the severity of the hypertension (for example –tachycardia where the heart rate is very high) the dosage is optimize or

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determined by one of ordinary skill in the art. One of ordinary skill in the art would have been motivated to use olmesartan medoximil/irbesartan and lercanidipine instead of telmisartan and lacidipine since olmesartan medoximil/irbesartan and lercanidipine is also taught by the above references.

Further, one of skill would have been motivated to combine the teachings of Gaviraghi, Sada, New Drug, Gasser and Norwood with that of PDR because the drugs in question are functionally similar to the drugs used by the above reference;

- a) angiotensin II receptor blocker
- b) calcium channel blocker

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00 Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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7/13/05


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